AUTOIMMUNE DISEASES

The immune system is essential to survival, and even a modest decrease in immune function can leave a person susceptible to infection. But the immune system itself can also *cause* disease, by inappropriately attacking the body's own organs, tissues, or cells.

More than 80 autoimmune diseases have been described to date. Some, such as type 1 diabetes, attack specific organs while others, such as systemic lupus erythematosus (SLE), involve multiple organs. Although many autoimmune diseases are rare, collectively they affect approximately 5 to 8 percent of the U.S. population. A disproportionate number of people with autoimmune disorders are women. For unknown reasons, the prevalence of autoimmune diseases is increasing.

NIAID's Division of Allergy, Immunology, and Transplantation (DAIT) supports a broad range of basic and clinical research programs in autoimmunity. Basic research focuses on understanding the genetics of autoimmunity, elucidating the mechanisms of self-tolerance, developing approaches to induce self-tolerance, and characterizing pathways of immune-mediated tissue destruction. Knowledge gained from basic research studies provides the rationale for clinical strategies to diagnose autoimmune diseases and to develop novel treatments for ongoing disease.

In response to congressional interest in autoimmune diseases, NIH established the Autoimmune Diseases Coordinating Committee (ADCC) in 1998 to coordinate research on autoimmune disorders. Participation in this committee is very broad and includes the directors, or their designees, of each of the NIH Institutes and Centers involved in autoimmune disease research; representatives of other Federal agencies, including the Centers for Disease Control and Prevention and the Food and Drug Administration, whose programs include health functions or responsibilities relevant to these diseases; and representatives from a number of private organizations concerned with autoimmune diseases.

As required by the Children's Health Act of 2000, ADCC prepared the Autoimmune Diseases Research Plan and presented it to Congress in late 2002. In March 2005, the ADCC submitted to Congress its third progress report,which summarized fiscal year (FY) 2003 NIH funding, research accomplishments, and programmatic activities in autoimmune diseases research. The report, "Progress in Autoimmune Diseases Research," is available to the public at *http://www.niaid.nih.gov/publications/pdf/ADCCFinal.pdf*.

In addition to its basic autoimmune research portfolio, DAIT supports several clinical research programs on autoimmune diseases. The Autoimmunity Centers of Excellence (ACEs) facilitate close interactions between clinicians and basic researchers to promote collaborative research on autoimmune diseases, including single-site and multisite pilot clinical trials of immunomodulatory therapies; this program recently expanded from four to nine centers. Numerous ongoing ACEs-supported clinical trials include a phase I/II clinical trial of anti-CD20 for treatment for lupus, a phase I clinical trial of anti-tumor necrosis factor for treatment of lupus nephritis, and a preclinical study of DNase treatment now underway with a follow-on phase Ib trial planned.

The Autoimmune Disease Prevention Centers conduct research on the development of new prevention strategies for autoimmune diseases and evaluate these approaches in pilot and clinical studies. In FY 2005, the centers supported 22 pilot projects to test innovative prevention approaches or methods to measure biomarkers of autoimmune disease progression.

NIAID, in partnership with the National Institute of Diabetes and Digestive and Kidney

Diseases, and the Juvenile Diabetes Research Foundation International, cosponsors the Immune Tolerance Network (ITN). This international consortium of more than 80 scientists and physicians is dedicated to the discovery and evaluation of methods that can induce stable, long-term immune tolerance in patients with many immune-mediated disorders, including autoimmune disorders. Tolerance strategies attempt to reprogram immune cells so they no longer attack the patient's own tissues, but are still able to effectively guard the body against infection. Because tolerance-inducing therapies would eliminate the need for lifelong immunosuppressive drug regimens—which themselves have serious side effects—they have the potential to revolutionize the management of many autoimmune diseases. The network has established several state-of-the-art core facilities and has supported 18 approved clinical protocols, as well as several additional studies of the immune mechanisms involved in tolerance. More information on ITN is available at *www.immunetolerance.org*.

Through the Clinical Trials Network for Stem Cell Transplantation for Autoimmune Diseases, NIAID developed clinical trials to assess the efficacy of hematopoietic stem cell transplantation to treat severe autoimmune diseases such as multiple sclerosis, SLE, and scleroderma. Studies of the underlying immune mechanisms of autoimmune diseases will be performed along with the clinical trials. More information about NIH clinical research studies is available at *www.clinicaltrials.gov*. These complex trials are expected to open in FY 2006. The consortium will also conduct studies of the underlying immune mechanisms of these diseases and treatments as the trials progress.

DAIT supports three genetics research resources for autoimmune diseases. The Multiple Autoimmune Disease Genetics Consortium collects clinical data and genetic material from families in which at least two individuals have two or more autoimmune diseases. The data and samples will be made available to researchers studying the genetics of susceptibility or resistance to autoimmune diseases. More information can be found at *www.madgc.org*.

The North American Rheumatoid Arthritis Consortium (NARAC) collects clinical data and genetic material from families with rheumatoid arthritis. These data are made available to investigators to facilitate the characterization of the genes underlying susceptibility to rheumatoid arthritis. NARAC is jointly supported by DAIT, the National Institute of Arthritis and Musculoskeletal and Skin Diseases, and the Arthritis Foundation. More information can be found at *www.naracdata.org*.

In FY 2005, NIAID, with co-sponsorship from NINDS, awarded five research cooperative agreements under the new program, Human Leukocyte Antigen (HLA) Region Genetics in Immune-Mediated Diseases. The objectives of this program are to define the association between HLA region genes or genetic markers and immune-mediated diseases, including risk and severity of disease and organ and cell transplantation outcomes. This program is the successor to the International Histocompatibility Working Group (IHWG). More information about the IHWG can be found at *http://www.ihwg.org*.

Although researchers have made considerable progress in understanding the immune mechanisms that mediate tissue injury in autoimmune diseases, much remains to be learned. In particular, scientists are studying the causes of these diseases, the genetic factors that make people susceptible to them, and the regulatory mechanisms that control autoantibody production. NIAID is committed to advancing the understanding of how and why autoimmune diseases occur, and to promoting the application of basic research to clinical investigations in order to develop more effective therapeutic approaches and prevention strategies.